Original Research Article

To study adrenal insufficiency and to determine relationship between BMI and serum cortisol levels in cirrhotic patients

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A B S T R A C T

Introduction: Liver cirrhosis is a major cause of mortality worldwide. Several studies reported that adrenal insufficiency (AI) is common in critically ill cirrhotic patients. However, there is scarcity of data on hepato-adrenal syndrome in cirrhotic patients. As this is an important complication of cirrhosis, this study is needed to know the profile of Adrenal Insufficiency in cirrhotic patients.

Aims and Objectives of the Study: 1. To study adrenal insufficiency in patients of cirrhosis. 2. To determine the relationship between BMI and serum cortisol levels.

Materials and Methods: 50 patients of cirrhosis admitted in medicine/gastroenterology ward of DMC&H, Ludhiana. Depending on the levels of cortisol, patients can be categorized into 3 groups. Clinically diagnosed patients of cirrhosis were included in our study whereas HIV/Immunodeficiency, Severe chronic heart disease, Chronic obstructive lung disease, Chronic hemodialysis, Severe sepsis, septic shock and patients on steroid therapy were excluded.

Results: AI was present in 14 (28%) patients of Cirrhosis. The difference between cortisol levels with respect to BMI was found to be statistically significant.

Conclusions: AI forms important part of spectrum of Cirrhosis and these patients should be evaluated for adrenal dysfunction.

1. Introduction

Relative adrenal insufficiency (RAI) is a syndrome characterized by decreased production of cortisol with respect to peripheral demands.[1]

Cortisol is a steroid hormone that regulates metabolism and immune system, maintenance of vascular tone and inhibition of production of proinflammatory cytokines and adhesion molecule expressions.[2]

Over 90% of circulating cortisol is bound to Corticosteroid binding globulin (CBG) (also called transcortin) and albumin, with less than 10% in the free biologically active form.[3]

To assess the severity of the liver disease, scoring models have been used. The oldest model is the Child-Pugh classification.[4]

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A recent model has been developed for the assessment of prognosis which is the Model of End-stage Liver Disease (MELD) score.[5] In this model there are only objective parameters, bilirubin, prothrombin time and creatinine. It is used to calculate mortality risk for patients with end-stage live r disease.[6,7]

The percentage of AI in cirrhotic patients varies among different studies and depends on different methods and criteria used to evaluate adrenal function.[8]

With SD-SST, the prevalence of AI in terminally ill cirrhotic patients varied between 10%[9] to 87%[10]

With LD-SST, the prevalence of AI in terminally ill cirrhotic patients varied between 33%[11] and 60%.[12]

Adrenal insufficiency (AI) has been described in all stages of cirrhotic patients.[13] However, the exact mechanism leading to AI in cirrhotic population is not yet known. It is known that cholesterol is an important substrate for steroid synthesis and adrenal glands synthesize cortisol

whenever is necessary. In cirrhosis, the adrenal glands synthesize the reduced amount of cortisol especially under stress conditions leading to "adrenal exhaustion syndrome" ending to AI.[14]

The mechanism of action of ACTH is through binding to a seven-membrane-spanning G protein-coupled ACTH receptor.[15]

Upon ligand binding, the receptor undergoes conformational changes that stimulate adenylyl cyclase, which further leads to an increase in intracellular cAMP and subsequent activation of protein kinase A. It stimulates lipoprotein uptake into cortical cells. This stimulates transcription of the genes coding for P450scc, steroid 11β-hydroxylase, and their associated electron transfer proteins.[16]

2. Aims and Objectives of the study

1. To study adrenal insufficiency in patients of cirrhosis.
2. To determine the relationship between BMI and serum cortisol levels.

3. Materials and Methods

3.1. Source of data

Patients admitted in medicine/gastroenterology ward of DMC&H

50 consecutive patients of cirrhosis were included in the study.

3.2. Inclusion criteria

Diagnosed patients of cirrhosis based on clinical/ biochemical / radiological/ endoscopy and or liver biopsy.

3.3. Exclusion criteria

1. HIV/Immunodeficiency
2. Severe chronic heart disease
3. Chronic obstructive lung disease
4. Chronic hemodialysis
5. Severe sepsis or septic shock.
6. Patients on steroid therapy

Depending upon the levels of cortisol, patients were divided into 3 groups:

Group I Patients having > 15 μg /dl cortisol (Baseline levels) n=31

Group II Patients having 3 -15 μg /dl cortisol (Baseline levels) n=11

Group III Patients having < 3 μg /dl cortisol (Baseline levels) n=8

In Group II, ACTH Stimulation (SD-SST) was done, then this Group was further divided into II a and II b

II a Patients having >18 μg /dl cortisol levels 30 minutes after ACTH stimulation (n=5)

II b Patients having <18 μg /dl cortisol levels 30 minutes after ACTH stimulation (n=6)

3.4. Diagnostic criteria for Adrenal Insufficiency

Levels of serum cortisol at 6-10 am $<3\mu$g/ dI confirms Adrenal Insufficiency.

Levels of serum cortisol at 6-10 am $>15\mu$g/ dI rules out Adrenal Insufficiency

Intermediate cortisol levels at 6-10 am are 3-15 μg/dl.

ACTH Stimulation were performed for intermediate cortisol levels. The diagnosis of adrenal insufficiency was considered if the serum cortisol level is $<18\mu$g/ dI, 30 minutes after stimulation.[17]

All the 50 patients were diagnosed on ultrasound findings.

Liver function tests were done in all the patients

Group A- CTP Score (5-6)

Group B- CTP Score (7-9)

Group C- CTP Score $\geq$ 10

3.5. MELD Score: Model for End-Stage Liver Disease.

3.8($\log_e$ serum bilirubin mg/dl) +11.2($\log_e$ INR) +9.6($\log_e$ serum creatinine mg/dl) +6.4.

3.6. Assay

Serum cortisol levels were determined by Electrochemiluminescence Immunoassay

3.7. Statistical analysis

The data was analyzed using Microsoft excel and SPSS version 20.0 (IBM SPSS, Chicago, Illinois). Mean and standard deviation were computed for the variables. The comparison between groups were done by Chi square and ANOVA. P value ≤ 0.005 was taken as significant.

3.8. Distribution of subjects according to adrenal function

Out of 50 patients included in this study, 14 (28%) patients had Adrenal Insufficiency

Out of 50 patients enrolled, 37 patients had BMI > 23. All the Adrenal insufficient patients had BMI ≥ 23. All the patients with BMI< 23 were in Group I. A significant relationship was found between cortisol levels and BMI (p=0.007).

4. Discussion

The prevalence of AI in Cirrhosis was 28% in our study. Acevedo et al[18] reported 26% AI. Galbois et al[19] reported 33% AI prevalence whereas other studies reported higher prevalence of AI.[20]

Table 1: Child-Turcotte-Pugh scoring system

Factor	Units	1	2	3
Serum bilirubin	mg/dl	1-1.9	2-2.9	>3
Serum albumin	g/dl	>3.5	2.8-3.5	<2.8
Prothrombin time / INR	Seconds	1-3 <1.7	4-6 1.7-2.3	>6 >2.3
Ascites		absent	Slight	Moderate
Hepatic encephalopathy	grade	none	1&2	3&4

Table 2: Distribution of subjects according to BMI

BMI	Group I	Group II a	Group II b	Group III	P value
<18.5 (n=3)	3 (9.67%)	0(0.00%)	0(0.00%)	0(0.00%)	
18.5 -22.9 (n=10)	10 (32.25%)	0(0.00%)	0(0.00%)	0(0.00%)	
23-24.9 (n=14)	7 (22.58%)	2(40.00%)	3(50.00%)	1(12.5%)	0.007
>25 (n=23)	11 (35.48%)	3(60.00%)	3(50.00%)	7(87.5%)	
MEAN ± SD	23.87 ± 4.23	26.1 ± 2.78	26.41 ± 3.78	30.34 ± 6.4	
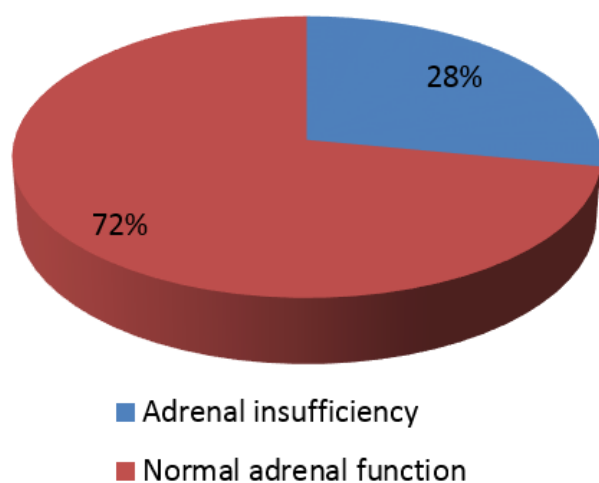
Fig. 1:

Prevalence varies according to choice of subjects in different studies. Higher prevalence of AI was found in studies that included subjects with liver failure, liver transplant recipients and critically ill cirrhotic patients as compared to studies with stable cirrhotic patients. The percentage of AI in cirrhotic patients varies among different studies and depends on the different methods used to estimate adrenal function.

Out of 50 patients enrolled, 37 patients had BMI > 23. All the Adrenal insufficient patients had BMI $\geq$ 23. All the patients with BMI< 23 were in Group I. A significant relationship was found between cortisol levels and BMI (p=0.007).

Higher the BMI, lesser the value of serum cortisol. Therefore there was inverse relationship between serum cortisol levels and BMI.

A cause- effect relationship between obesity and cortisol levels is not clearly known, it may be either due to altered hypothalamic-pituitary-adrenal axis in obesity or due to enchanced metabolic clearance of cortisol in obesity.

5. Conclusion

We concluded that AI forms important part of spectrum of Chronic liver disease and these patients should be evaluated for adrenal dysfunction periodically.

6. Source of funding

None.

7. Conflict of interest

None.

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Author biography

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